



IFW

PATENT  
Attorney Docket No. LEX-010C1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT(S): Gillies *et al.* CONFIRMATION NO.: 8576  
SERIAL NO.: 10/603,064 GROUP NO.: 1646  
FILING DATE: June 24, 2003 EXAMINER: Mertz, P.  
TITLE: Multiple Cytokine Protein Complexes

**CERTIFICATE OF FIRST CLASS MAILING UNDER 37 C.F.R. 1.8**

I hereby certify that this correspondence, and any document(s) referred to as enclosed herein, are being deposited with the United States Postal Service as first class mail, postage prepaid, in an envelope addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 1st day of June, 2005.

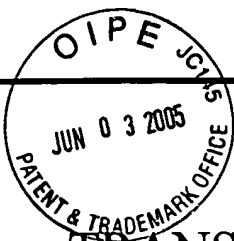
  
\_\_\_\_\_  
Lisa Marie Solis

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Submitted herewith are:

1. Transmittal Form (1 page);
2. Supplemental Information Disclosure Statement (2 pages);
3. Form PTO – 1449 (4 pages);
4. Copy of cited references B82-B87 and C219-C259; and
5. Return receipt postcard.



# TRANSMITTAL FORM

Application Serial Number	10/603,064
Filing Date	June 24, 2003
First Named Inventor	Gillies
Group Art Unit	1646
Examiner Name	Mertz, P.
Attorney Docket No.	LEX-010C1
Patent No.	Not applicable
Issue Date	Not applicable

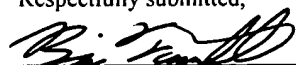
## ENCLOSURES (check all that apply)

<input type="checkbox"/> Fee Transmittal Form  <input type="checkbox"/> Check Attached <input type="checkbox"/> Copy of Fee Transmittal Form	<input type="checkbox"/> Copy of Notice to File Missing Parts of Application  <input type="checkbox"/> Formal Drawing(s)	<input type="checkbox"/> Notice of Appeal to Board of Patent Appeals and Interferences  <input type="checkbox"/> Appeal Brief (in triplicate)
<input type="checkbox"/> Amendment/Response  <input type="checkbox"/> Preliminary <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Letter to Official Draftsperson including Drawings [Total Sheets ____]	<input type="checkbox"/> Request For Continued Examination (RCE) Transmittal  <input type="checkbox"/> Power of Attorney (Revocation of Prior Powers)  <input type="checkbox"/> Terminal Disclaimer	<input type="checkbox"/> Status Inquiry  <input checked="" type="checkbox"/> Return Receipt Postcard <input checked="" type="checkbox"/> Certificate of First Class Mailing under 37 C.F.R. 1.8  <input type="checkbox"/> Certificate of Facsimile Transmission under 37 C.F.R. 1.8
<input type="checkbox"/> Petition for Extension of Time	<input type="checkbox"/> Executed Declaration and Power of Attorney for Utility or Design Patent Application	<input type="checkbox"/> Additional Enclosure(s) (please identify below)
<input checked="" type="checkbox"/> Supplemental Information Disclosure Statement <input checked="" type="checkbox"/> Form PTO-1449 <input checked="" type="checkbox"/> Copies of IDS Citations B82-B87 and C219-C259	<input type="checkbox"/> Small Entity Statement  <input type="checkbox"/> CD(s) for large table or computer program	
<input type="checkbox"/> Certified Copy of Priority Document(s)	<input type="checkbox"/> Amendment After Allowance	
<input type="checkbox"/> Sequence Listing submission <input type="checkbox"/> Paper Copy/CD <input type="checkbox"/> Computer Readable Copy <input type="checkbox"/> Statement verifying identity of above	<input type="checkbox"/> Request for Certificate of Correction <input type="checkbox"/> Certificate of Correction (in duplicate)	

## CORRESPONDENCE ADDRESS

Direct all correspondence to: Patent Administrator  
Kirkpatrick & Lockhart Nicholson  
Graham LLP  
75 State Street  
Boston, MA 02109-1808  
Tel. No.: (617) 261-3100  
Fax No.: (617) 261-3175

## SIGNATURE BLOCK

Respectfully submitted,  
  
Brian A. Fairchild  
Attorney for Applicants  
Kirkpatrick & Lockhart Nicholson  
Graham LLP  
75 State Street  
Boston, MA 02109-1808

Date: June 1, 2005  
Reg. No. 48,645  
Tel. No.: (617) 261-3169  
Fax No.: (617) 261-3175



PATENT  
Attorney Docket No. LEX-010C1

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

APPLICANT(S): Gillies *et al.* CONFIRMATION NO.: 8576  
SERIAL NO.: 10/603,064 GROUP NO.: 1646  
FILING DATE: June 24, 2003 EXAMINER: Mertz, P.  
TITLE: Multiple Cytokine Protein Complexes

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

Sir:

In accordance with the provisions of 37 C.F.R. 1.97 and 1.98, Applicants hereby make of record the patents and publications listed on the accompanying Form PTO-1449, and other information contained herein, for consideration by the Examiner in connection with the examination of the above-identified patent application. Copies of the non-U.S. patent documents and non-patent publications are enclosed.

**REMARKS**

In accordance with the provisions of 37 C.F.R. 1.97, this statement is being filed (CHECK ONE):

- ☒ (1) within three (3) months of the **filing date** of a national application other than a continued prosecution application under 37 C.F.R. 1.53(d), or within three (3) months of the **date of entry of the national stage** as set forth in 37 C.F.R. 1.491 in an international application, or before the mailing of the **first Office action** on the merits, or before the mailing of a **first Office action** after the filing of a request for continued examination under 37 C.F.R. 1.114; or
- ☐ (2) after the period defined in (1) above but before the mailing date of any of a **final action** under 37 C.F.R. 1.113, a **notice of allowance** under 37 C.F.R. 1.311, or an action that otherwise closes prosecution in the application, and
- ☐ the requisite Statement is below, **OR**
- ☐ the requisite fee under 37 C.F.R. 1.17(p), namely **\$180.00**, is included herein; or

- ☐ (3) after the period defined in (2) above but before the payment of the **issue fee**, **AND**
- ☐ the requisite Statement is below, **AND**
- ☐ the requisite petition fee under 37 C.F.R. 1.17(p), namely **\$180.00** is included herein.

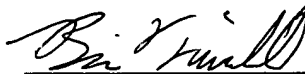
It is respectfully requested that each of the patents and publications listed on the attached Form PTO-1449, and other information contained herein, be made of record in this application.

Applicants believe no fee is required. If a fee is required, please debit deposit account 50-1721.

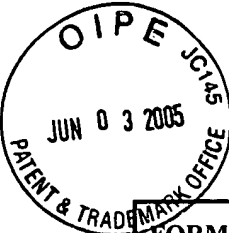
Date: June 1, 2005  
Reg. No. 48,645

Tel. No.: (617) 261-3169  
Fax No.: (617) 261-3175

Respectfully submitted,



Brian A. Fairchild  
Attorney for Applicants  
Kirkpatrick & Lockhart Nicholson  
Graham LLP  
75 State Street  
Boston, Massachusetts 02109-1808



<b>FORM PTO - 1449</b>				<b>ATTORNEY DOCKET NO.:</b> LEX-010C1					
<b>INFORMATION DISCLOSURE STATEMENT</b>				<b>APPLICANT(S):</b> Gillies <i>et al.</i>					
				<b>SERIAL NO.:</b> 10/603,064					
				<b>FILING DATE:</b> June 24, 2003					
				<b>GROUP NO.:</b> 1646					
<b>U.S. PATENT DOCUMENTS</b>									
<b>EXAM. INIT.</b>		<b>DOCUMENT NUMBER</b>	<b>DATE</b>	<b>NAME</b>	<b>CLASS</b>	<b>SUB CLASS</b>	<b>FILING DATE IF APPROPRIATE</b>		
	A100	4,732,683	3/22/88	Georgiades <i>et al.</i>					
	A101	4,737,462	4/12/88	Mark <i>et al.</i>					
	A102	5,082,658	1/21/92	Palladino					
	A103	5,091,513	2/25/92	Huston <i>et al.</i>					
	A104	5,399,346	3/21/95	Anderson <i>et al.</i>					
	A105	5,428,130	6/27/95	Capon <i>et al.</i>					
	A106	5,795,779	8/18/98	McCormick					
	A107	5,827,703	10/27/98	Debs <i>et al.</i>					
	A108	6,627,615	9/30/03	Debs <i>et al.</i>					
	A109	2004/0180035	9/16/04	Gillies <i>et al.</i>					
	A110	2004/0180386	9/16/04	Carr <i>et al.</i>					
	A111	2004/0203100	10/04/04	Gillies <i>et al.</i>					
<b>FOREIGN PATENT DOCUMENTS</b>									
<b>EXAM. INIT.</b>		<b>DOCUMENT NUMBER</b>	<b>DATE</b>	<b>COUNTRY CODE</b>	<b>CLASS</b>	<b>SUB CLASS</b>	<b>FILING DATE</b>	<b>ABSTRACT ONLY</b>	<b>ENGLISH LANG (Y/N)</b>
	B82	0 428 596 B1	4/17/96	EP					Y
	B83	0 433 827 B1	3/4/98	EP					Y
	B84	WO 92/10755	6/25/92	PCT					Y
	B85	WO 94/25609	11/10/94	PCT					
	B86	WO 98/52976	11/26/98	PCT					
	B87	WO 02/074783		PCT					Y
<b>EXAMINER</b>					<b>DATE CONSIDERED</b>				

<b>FORM PTO - 1449</b> <b>INFORMATION DISCLOSURE STATEMENT</b>		ATTORNEY DOCKET NO.: LEX-010C1 APPLICANT(S): Gillies <i>et al.</i> SERIAL NO.: 10/603,064 FILING DATE: June 24, 2003 GROUP NO.: 1646
<b>OTHER ART, JOURNAL ARTICLES, ETC.</b>		
<b>EXAM. INIT.</b>	<b>OTHER DOCUMENTS: (Including Author, Title, Date, Relevant Pages, Place of Publication)</b>	
	C219	Anderson <i>et al.</i> , (1994), "Effects of Route and Formulation on Clinical Pharmacokinetics of Interleukin-2," Clin. Pharmacokinet., 27(1):19-31.
	C220	Barbulescu <i>et al.</i> , (1998), "IL-12 and IL-18 Differentially Regulate the Transcriptional Activity of the Human IFN- $\gamma$ Promoter in Primary CD4+ T Lymphocytes," J. Immunol., 160:3642-7.
	C221	Benacerraf <i>et al.</i> , (1959), "The Clearance of Antigen Antibody Complexes from the Blood by the Reticulo-Endothelial System," J. Immunol., 82:131-7.
	C222	Boulianne <i>et al.</i> , (1984), "Production of Functional Chimaeric Mouse/Human Antibody," Nature, 312:643-6.
	C223	Bubenik <i>et al.</i> , (1995), "Interleukin-2 Gene Therapy of Residual EL-4 Leukaemia Potentiates the Effect of Cyclophosphamide Pretreatment," J. Cancer Res. Clin. Oncol., 121:39-43.
	C224	Chan <i>et al.</i> , (1992), "Mechanisms of IFN- $\gamma$ Induction by Natural Killer Cell Stimulatory Factor (NKSF/IL-12). Role of Transcription and mRNA Stability in the Synergistic Interaction Between NKSF and IL-2," J. Immunol., 148:92-98.
	C225	Cohen <i>et al.</i> , (1998), "An Artificial Cell-Cycle Inhibitor Isolated from a Combinatorial Library," Proc. Natl. Acad. Sci. USA, 95:14272-7.
	C226	Connor <i>et al.</i> , (2004), "Ex vivo Evaluation of Anti-EpCAM Immunocytokine huKS-IL2 in Ovarian Cancer," J. Immunotherapy, 27:211-219.
	C227	Desai <i>et al.</i> , (1992), "IL-12 Receptor. II. Distribution and Regulation of Receptor Expression," J. Immunol., 148:3125-32.
	C228	Farner <i>et al.</i> , (1995), "Distinction Between $\gamma_c$ C Detection and Function in YT Lymphoid Cells and in the Granulocyte-Macrophage Colony-Stimulating Factor-Responsive Human Myeloid Cell Line, Tf-1," Blood, 86:4568-78.
	C229	Gurewich <i>et al.</i> , (1988), "Characterization of the Intrinsic Fibrinolytic Properties of Pro-Urokinase Through a Study of Plasmin-Resistant Mutant Forms Produced by Site-Specific Mutagenesis of Lysine," J. Clin. Invest., 82:1956-1962.
	C230	Hashimoto <i>et al.</i> , (1999), "Differential Antitumor Effects of Administration of Recombinant IL-18 or Recombinant IL-12 are Mediated Primarily by Fas-Fas Ligand- and Perforin-Induced Tumor Apoptosis, Respectively," J. Immunol., 163:583-9.
	C231	Hori <i>et al.</i> , (1987), "Establishment of an Interleukin 2-Dependent Human T Cell Line from a Patient with T Cell Chronic Lymphocytic Leukemia Who is Not Infected with Human T Cell Leukemia/Lymphoma Virus," Blood, 70:1069-72.
<b>EXAMINER</b>		<b>DATE CONSIDERED</b>

<b>FORM PTO - 1449</b>		<b>ATTORNEY DOCKET NO.:</b> LEX-010C1	
<b>INFORMATION DISCLOSURE STATEMENT</b>		<b>APPLICANT(S):</b> Gillies <i>et al.</i>	
		<b>SERIAL NO.:</b> 10/603,064	
		<b>FILING DATE:</b> June 24, 2003	
		<b>GROUP NO.:</b> 1646	
<b>OTHER ART, JOURNAL ARTICLES, ETC.</b>			
<b>EXAM. INIT.</b>	<b>OTHER DOCUMENTS: (Including Author, Title, Date, Relevant Pages, Place of Publication)</b>		
	C232	Karpusas <i>et al.</i> , (1997), "The Crystal Structure of Human Interferon $\beta$ at 2.2-A Resolution," <u>Proc. Natl. Acad. Sci. USA</u> , 94:11813-11818.	
	C233	Kelner <i>et al.</i> , (1994), "Lymphotactin: A Cytokine that Represents a New Class of Chemokine," <u>Science</u> , 266:1395-9.	
	C234	Kirkman <i>et al.</i> , (1989), "Prolongation of Cardiac Allograft Survival in Murine Recipients Treated with a Diphtheria Toxin-Related Interleukin-2 Fusion Protein," <u>Transplantation</u> , 47(2):327-330.	
	C235	Lawn <i>et al.</i> , (1981), "DNA Sequence of a Major Human Leukocyte Interferon Gene," <u>Proc. Natl. Acad. Sci. USA</u> , 78:5435-9.	
	C236	Lode <i>et al.</i> , (1998), "Gene Therapy with a Single Chain Interleukin 12 Fusion Protein Induces T Cell-Dependent Protective Immunity in a Syngeneic Model of Murine Neuroblastoma," <u>Proc. Natl. Acad. Sci. USA</u> , 95:2475-80.	
	C237	Lotze <i>et al.</i> , (1996), "Cytokine Gene Therapy of Cancer Using Interleukin-12: Murine and Clinical Trials," <u>Ann. NY Acad. Sci.</u> , 795:440-54.	
	C238	MacLean <i>et al.</i> , (1996), "Enhancing the Effect of Theratope STn-KLH Cancer Vaccine in Patients with Metastatic Breast Cancer by Pretreatment with Low-Dose Intravenous Cyclophosphamide," <u>J. Immunother.</u> , 19(4):309-316.	
	C239	Maghazachi <i>et al.</i> , (1997), "Interferon-Inducible Protein-10 and Lymphotactin Induce the Chemotaxis and Mobilization of Intracellular Calcium in Natural Killer Cells through Pertussis Toxin-Sensitive and -Insensitive Heterotrimeric G-Proteins," <u>FASEB J.</u> , 11:765-74.	
	C240	McMahan <i>et al.</i> , (1991), "A Novel IL-1 Receptor, Cloned From B-Cells by Mammalian Expression is Expressed in Many Cell Types," <u>EMBO J.</u> , 10:2821-32.	
	C241	Mehrotra <i>et al.</i> , (1993), "Effects of IL-12 on the Generation of Cytotoxic Activity in Human CD8+ T Lymphocytes," <u>J. Immunol.</u> , 151:2444-52.	
	C242	Miyake <i>et al.</i> , (1988), "Synthesis of Recombinant Human Single-Chain Urokinase-Type Plasminogen Activator Variants Resistant to Plasmin and Thrombin," <u>J. Biochem.</u> , 104:643-647.	
	C243	Mueller <i>et al.</i> , (1990), "Enhancement of Antibody-Dependent Cytotoxicity With A Chimeric Anti-GD2 Antibody," <u>J. Immunology</u> , 144(4):1382-1386	
	C244	Mullins <i>et al.</i> , (1998), "Interleukin-12 Overcomes Paclitaxel-Mediated Suppression of T-Cell Proliferation," <u>Immunopharmacol. Immunotoxicol.</u> , 20(4):473-492.	
	C245	Nastala <i>et al.</i> , (1994), "Recombinant IL-12 Administration Induces Tumor Regression in Association with IFN- $\gamma$ Production," <u>J. Immunol.</u> , 153:1697-706.	
<b>EXAMINER</b>		<b>DATE CONSIDERED</b>	

FORM PTO - 1449 INFORMATION DISCLOSURE STATEMENT		ATTORNEY DOCKET NO.: LEX-010C1 APPLICANT(S): Gillies <i>et al.</i> SERIAL NO.: 10/603,064 FILING DATE: June 24, 2003 GROUP NO.: 1646
OTHER ART, JOURNAL ARTICLES, ETC.		
EXAM. INIT.	OTHER DOCUMENTS: (Including Author, Title, Date, Relevant Pages, Place of Publication)	
	C246	Nelles <i>et al.</i> , (1987), "Characterization of Recombinant Human Single Chain Urokinase-Type Plaminogen Activator Mutants Produced by Site-Specific Mutagenesis of Lysine 158," <u>J. Biol. Chem.</u> , 262(12):5682-5689.
	C247	Palucka <i>et al.</i> , (1998), "Dendritic Cells as the Terminal Stage of Monocyte Differentiation," <u>J. Immunol.</u> , 160:4587-95.
	C248	Perussia <i>et al.</i> , (1992), "Natural Killer (NK) Cell Stimulatory Factor or IL-12 Has Differential Effects on the Proliferation of TCR- $\alpha\beta$ +, TCR- $\gamma\delta$ + T Lymphocytes, and NK Cells," <u>J. Immunol.</u> , 149:3495-502.
	C249	Radhakrishnan <i>et al.</i> , (1996), "Zinc Mediated Dimer of Human Interferon- $\alpha_{2b}$ Revealed by X-Ray Crystallography," <u>Structure</u> 4(12):1453-63.
	C250	Robinson <i>et al.</i> , (1998), "Optimizing the Stability of Single-Chain Proteins by Linker Length and Composition Mutagenesis," <u>Proc. Natl. Acad. Sci. USA</u> , 95:5929-34.
	C251	Runkel <i>et al.</i> , (1998), "Structural and Functional Differences Between Glycosylated and Non-Glycosylated Forms of Human Interferon- $\beta$ (IFN- $\beta$ )," <u>Pharmaceutical Res.</u> , 15:641-649.
	C252	Sharp <i>et al.</i> , (1988), "Codon Usage Patterns in <i>Escherichia coli</i> , <i>Bacillus subtilis</i> , <i>Saccharomyces cerevisiae</i> , <i>Schizosaccharomyces pombe</i> , <i>Drosophila melanogaster</i> and <i>Homo sapiens</i> ; a Review of the Considerable Within-Species Diversity," <u>Nucleic Acids Res.</u> , 16(17):8207-8211.
	C253	Taniguchi <i>et al.</i> , (1980), "Expression of the Human Fibroblast Interferon Gene in <i>Escherichia Coli</i> ," <u>Proc. Natl. Acad. Sci. USA</u> , 77:5230-5233.
	C254	Thurner, (1999), "Generation of Large Numbers of Fully Mature and Stable Dendritic Cells from Leukapheresis Products for Clinical Application," <u>J. Immunol. Methods</u> , 223:1-15.
	C255	Tiruppathi <i>et al.</i> , (1996), "Isolation and Characterization of a Cell Surface Albumin-Binding Protein from Vascular Endothelial Cells," <u>Proc. Nat. Acad. Sci. USA</u> , 93:250-4.
	C256	Voest <i>et al.</i> , (1995), "Inhibition of Angiogenesis in Vivo by Interleukin 12," <u>J. Natl. Canc. Inst.</u> , 87:581-6.
	C257	Weitkamp <i>et al.</i> , (1973), "Additional Data on the Population Distribution of Human Serum Albumin Genes; Three New Variants," <u>Ann. Hum. Genet.</u> , 37:219-26.
	C258	Wysocka <i>et al.</i> , (1995), "Interleukin-12 is Required for Interferon- $\gamma$ Production and Lethality in Lipopolysaccharide-Induced Shock in Mice," <u>Eur. J. Immunol.</u> , 25:672-6.
	C259	Yeh <i>et al.</i> , (1992), "Design of Yeast-Secreted Albumin Derivatives for Human Therapy: Biological and Antiviral Properties of a Serum Albumin-CD4 Genetic Conjugate," <u>Proc. Natl. Acad. Sci. USA</u> , 89:1904-8.
EXAMINER		DATE CONSIDERED